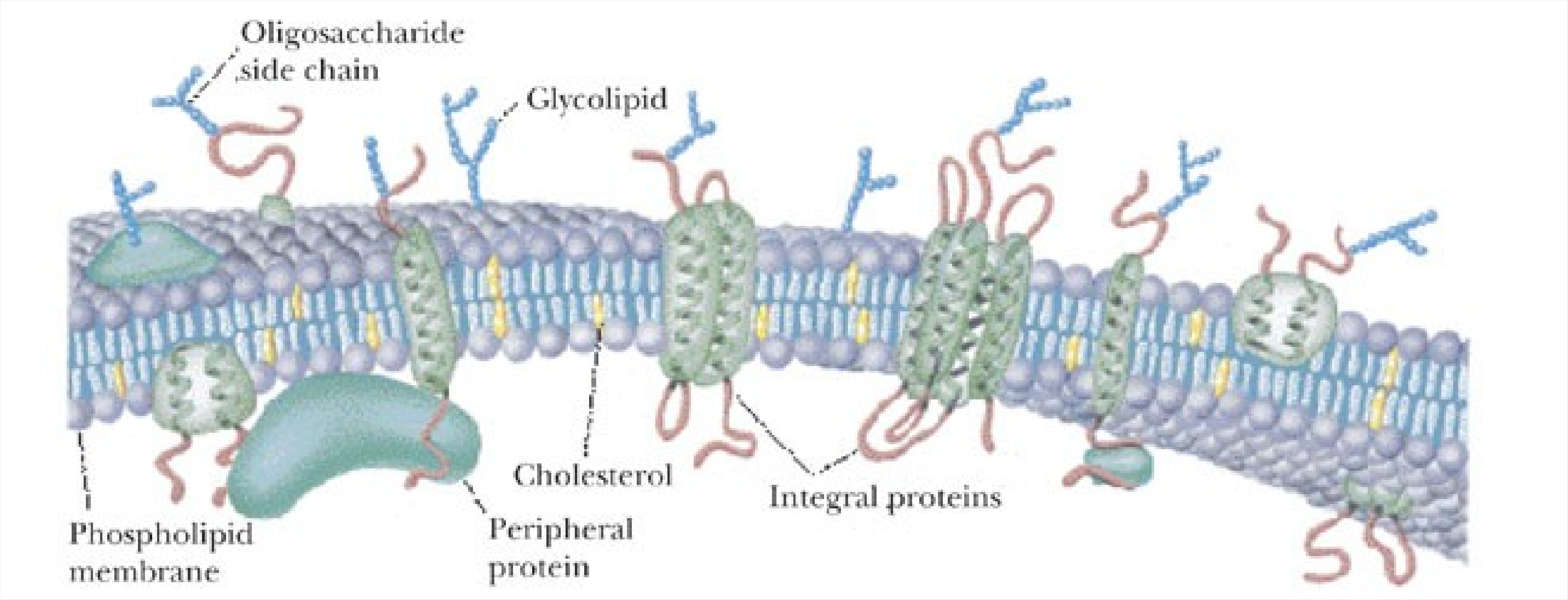
Chapter 12: Membranes

Voet & Voet:
Pages 390-415

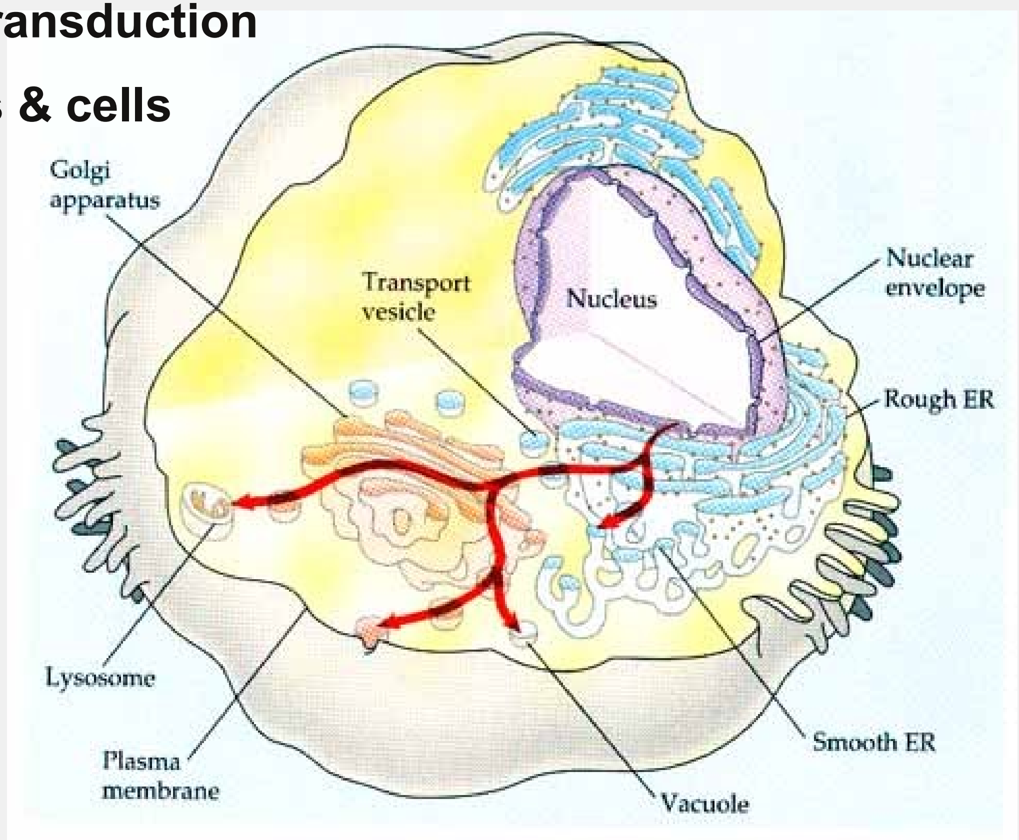


Membranes

Essential components of all living cells (define boundry of cells)

- exclude toxic ions and compounds; accumulation of nutrients
- energy transduction; cell locomotion
- reproductive processes; signal transduction
- varied interaction with molecules & cells

Some of the membranes present in a eucaryotic cell



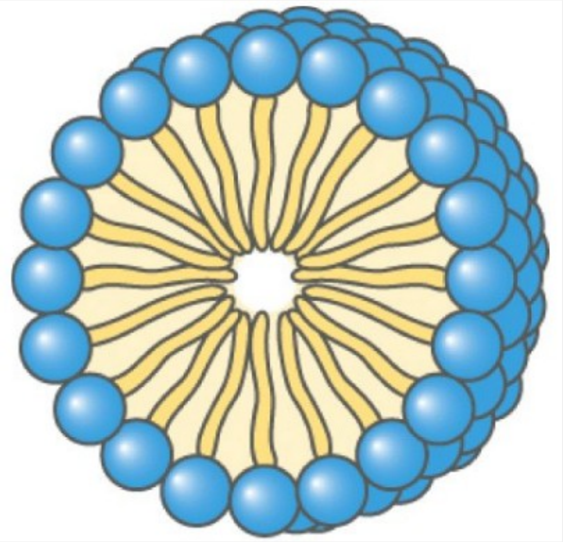
Simple Lipid Monolayers

Single Tailed lipids form micelles in H_2O

- globular (spherical) aggregates whose hydrocarbons tails are out of contact with water (similar to soaps and detergents)
- Eliminates unfavorable contacts between water and the hydrophobic tails AND permits solvation of polar head groups

Micelle formation is a cooperative process

- an assembly of a just a few lipids cannot shield their tails from the solvent
- in dilute solutions lipids do not form micelles until their concentration surpasses a ***critical micelle concentration*** *(cmc)*
- above the cmc almost all added lipids aggregate to form micelles

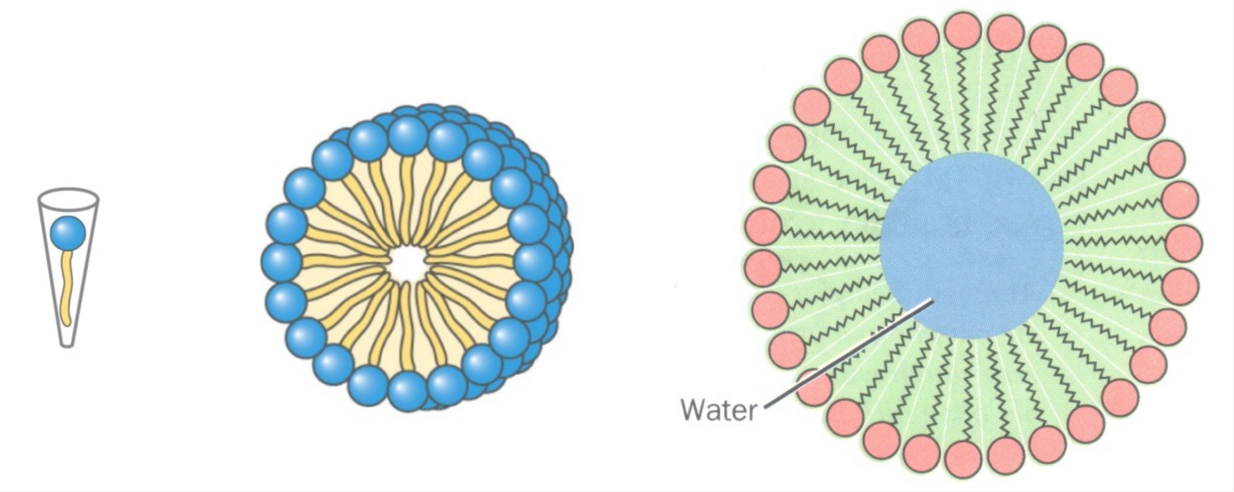


Micelle composed of single tailed lipids

Micelle Size & Shape

Geometric shape of lipid dictates optimal size & shape

- single tailed lipids have a conical van der Waal's surface
- efficiently packs into a spheroidal micelle with an ~ constant number of molecules (typically several hundred)
- larger micelles would have an internal water filled cavity (energetically unfavorable)



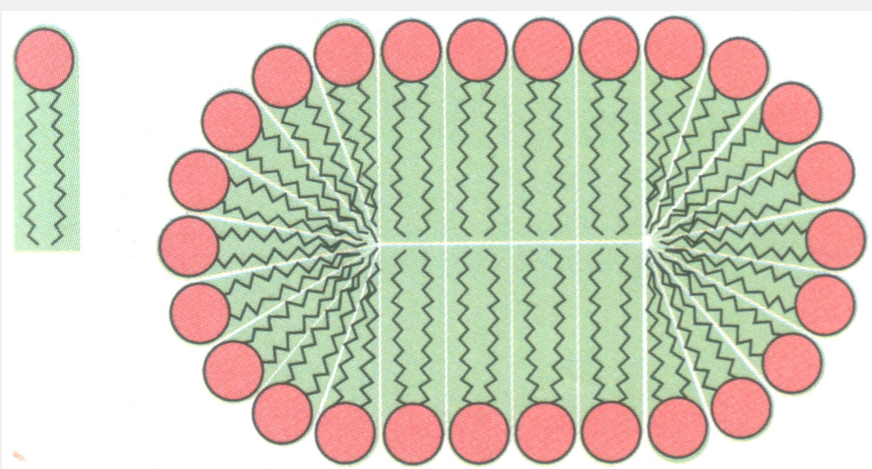
Typical Micelle

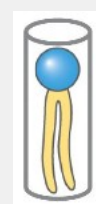
Energetically Unfavorable
(does not occur normally)

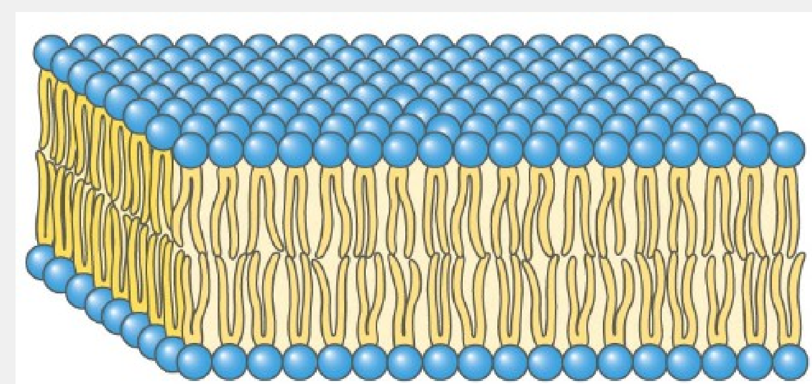
Simple Bilayers

Glycerophospholipids and Sphingolipids are two tailed lipids

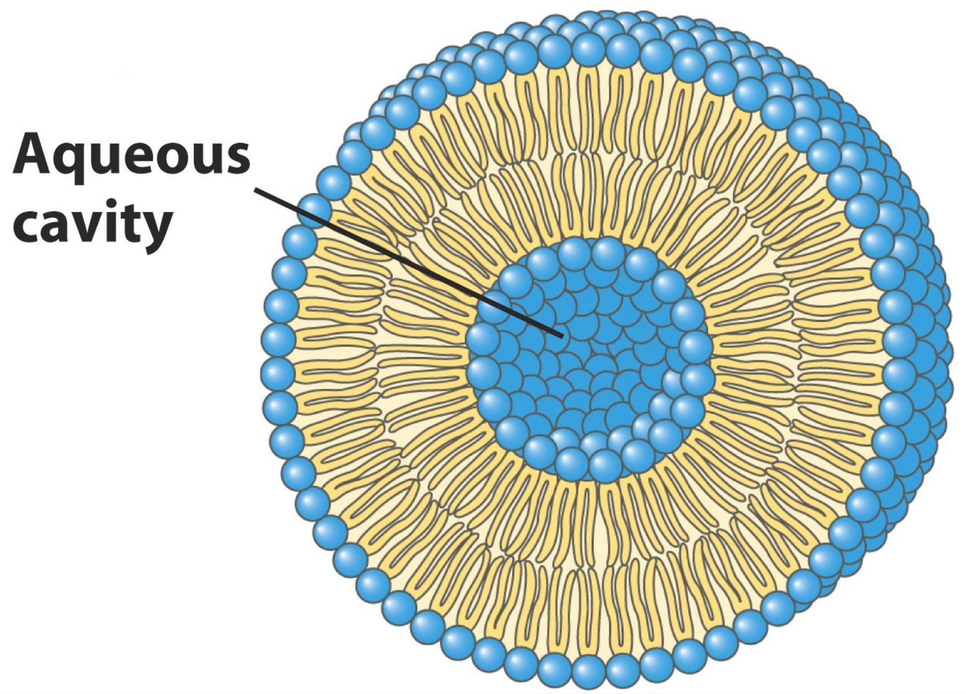
- two tailed lipids have a roughly cylindrical van der Waal's surface and preferentially form disc-shaped micelles
- Physical studies (Electron Microscopy & Small Angle X-ray Scattering) indicate the hydrophobic tails are almost fully extended
  - 60 Å cross section – length of one lipid ~30 Å when fully extended







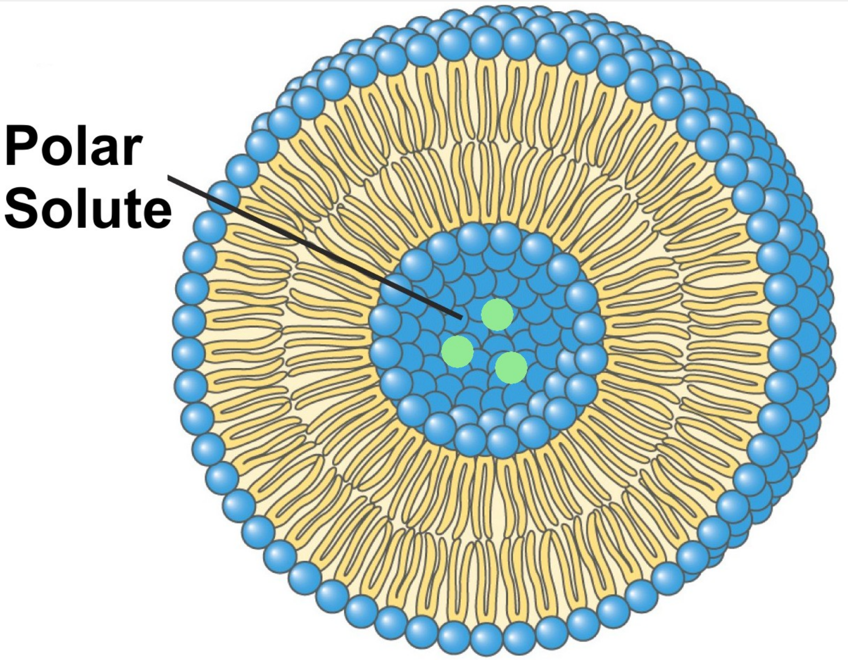
Liposomes



Phospholipid suspensions in water form multilamellar vesicles

- sonication generates liposomes
- generally from 100's – 1000 Å in diameter
  - central cavity filled with solvent similar to biological membranes
- once formed, liposomes are stable and can be isolated
  - important tool for studying membrane behavior

Liposomes



Lipid bilayers are impermeable to most polar substance

- sonication in presence of polar substance forms liposomes with polar compound in interior
  - polar compounds do not escape when liposomes are dialysed
- (surprisingly) water can traverse bilayers

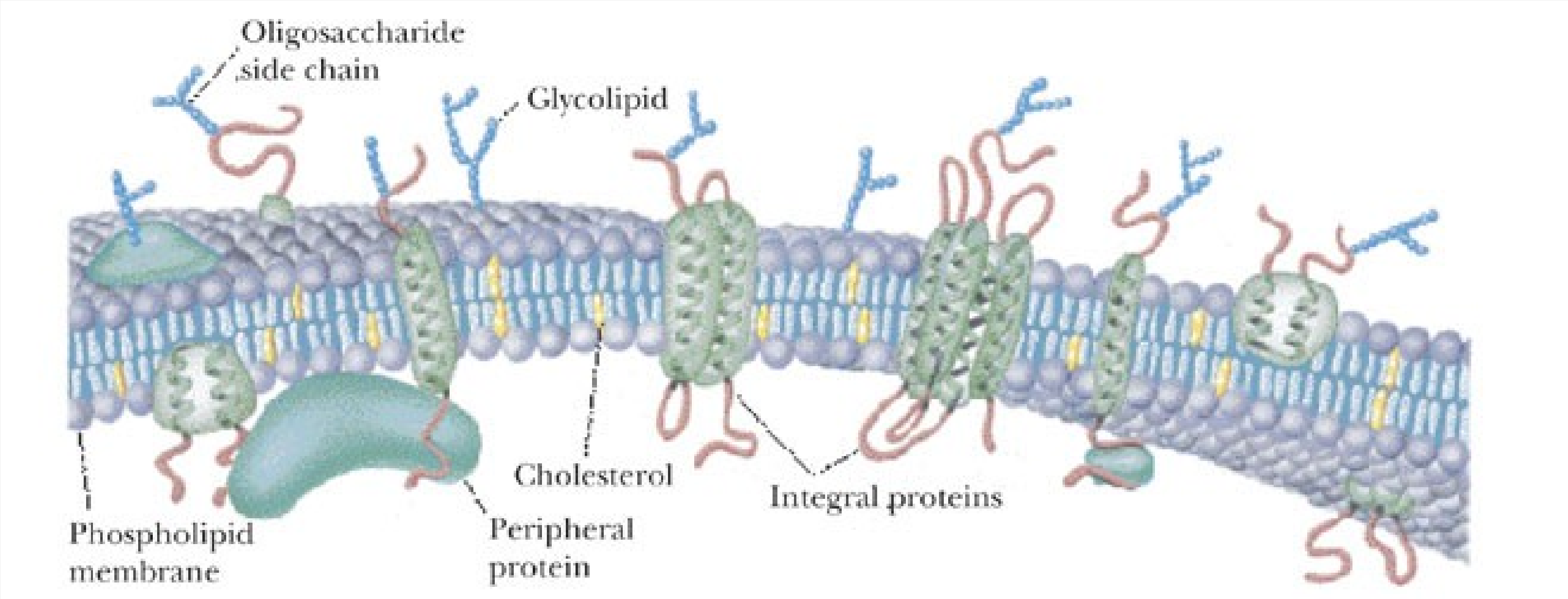
Liposomes are a promising vehicle for "drug" delivery

- requires ability to target vesicles to cells

Fluid Mosaic Model of Membranes

Singer & Nicholsen propose Fluid Mosaic Model of Membranes

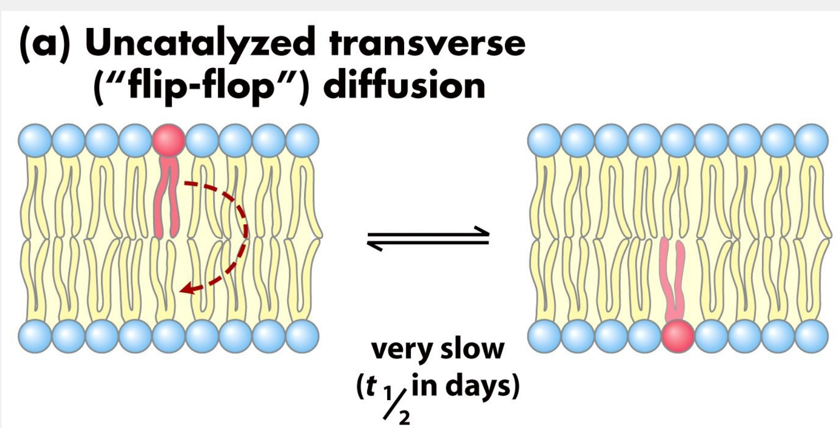
- membranes are dynamic structures
- lipids and proteins are free to move in 2D

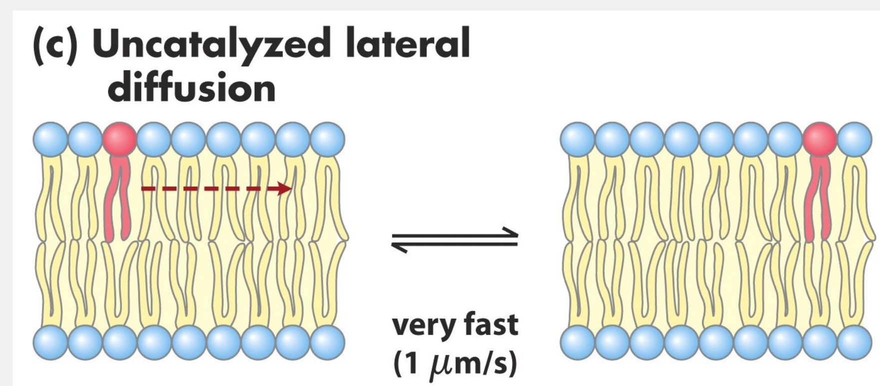


Lipid Bilayer

Bilayers are best described as two-dimensional fluids

- lipid transfer across the membrane is rare (transverse diffusion or 'flip-flop')
- lipids are highly mobile in the plane of the bilayer (lateral diffusion)

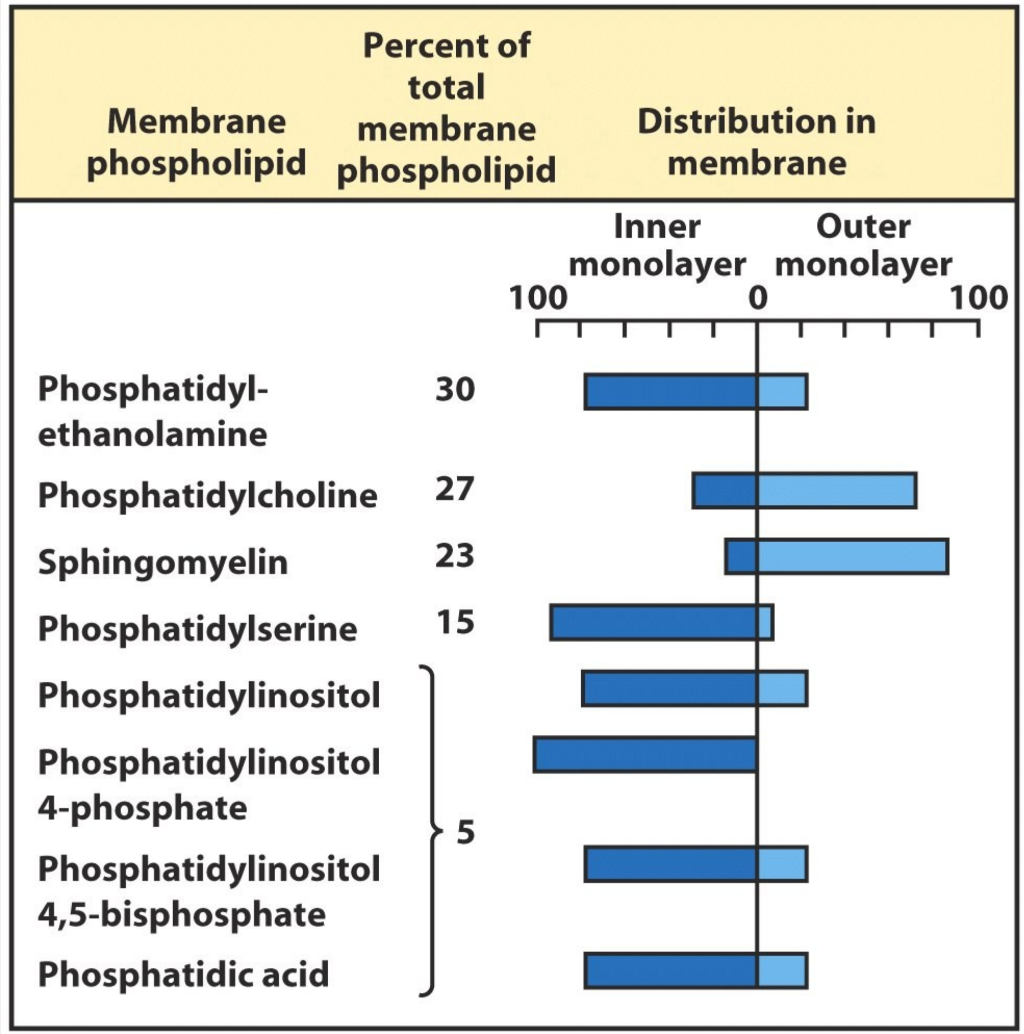




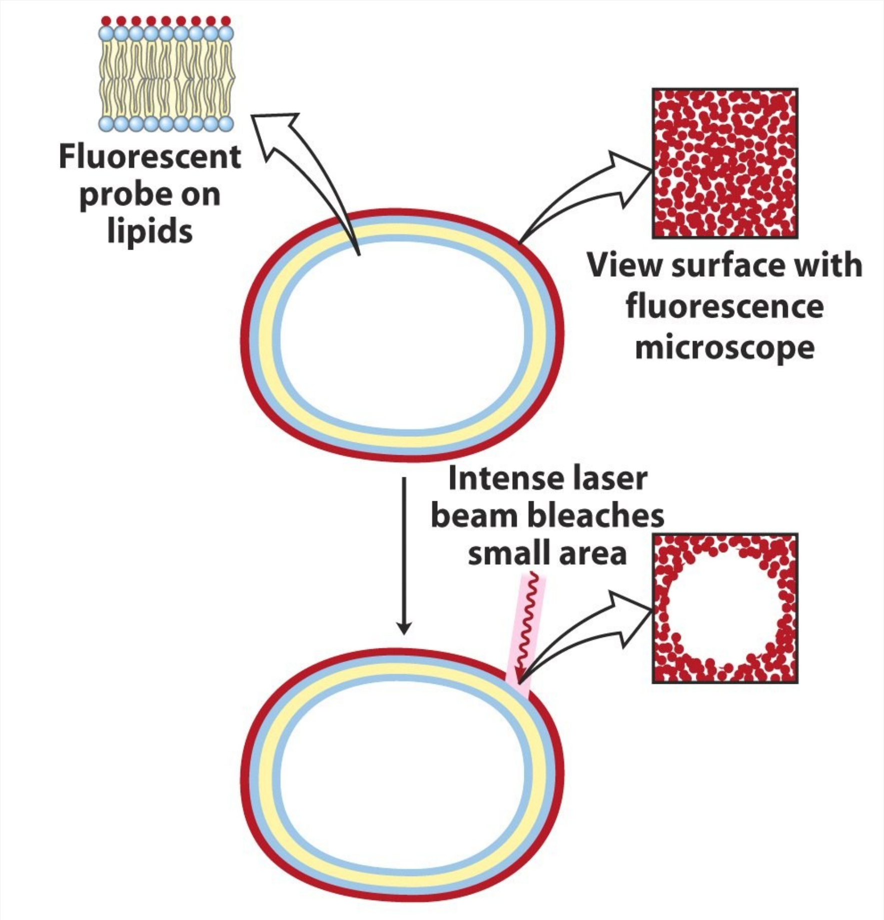
Asymmetric Lipid Distributions

In biological membranes, the slow rate of transverse diffusion contributes to the asymmetric distribution of lipids

- consequently, the inner and outer membrane monolayers have different properties

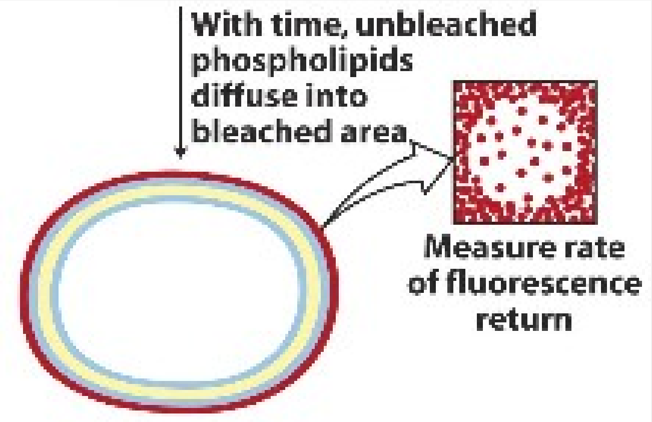


Evidence for Lateral Diffusion



Photobleaching Experiment

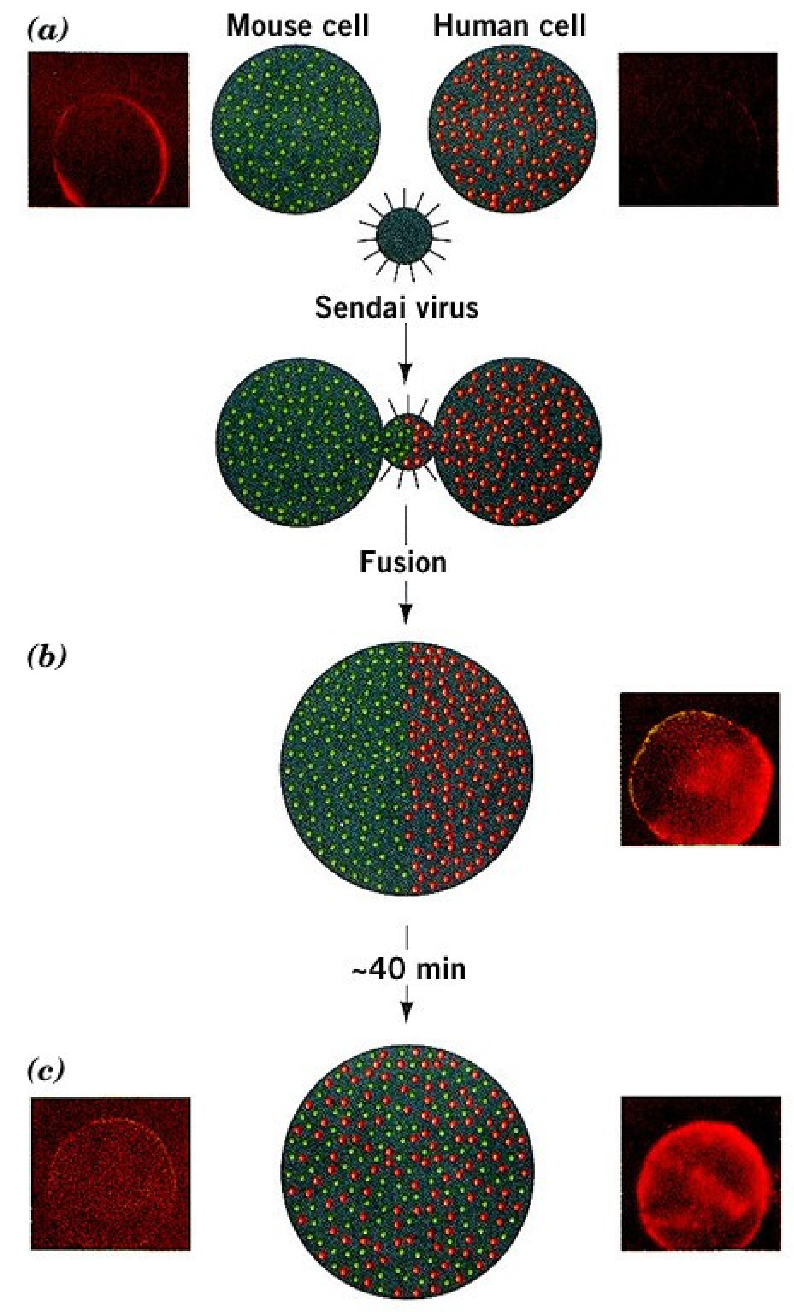
- Can observe lateral diffusion of labeled lipids as a function of time



More Evidence

A second experiment showing lateral diffusion in bilayers

- separate cells are labeled with distinct fluorophores
- cell membranes are fused
- fluorophore movement is observed as function of time



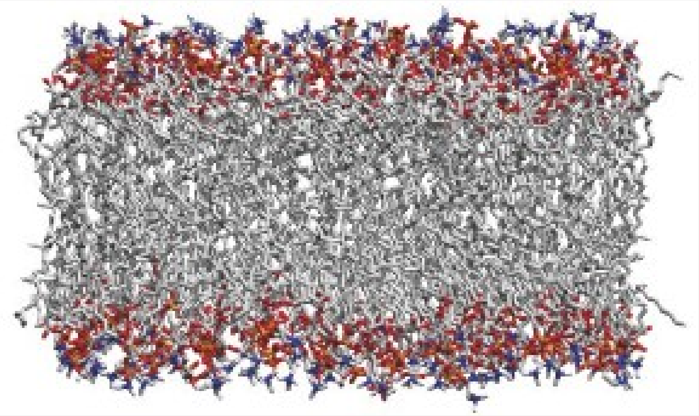
Bilayers and Temperature

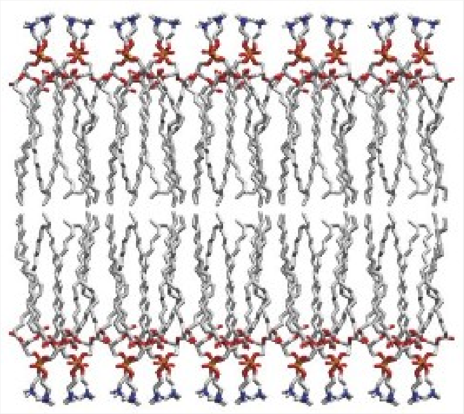
Below a characteristic transition temperature, bilayer undergo a sort of phase change called the **order-disorder transition**

- below the transition temperature, bilayers become a gel-like solid and lose their fluidity
  - average spacing between hydrocarbon tails is reduced from 4.6 to 4.2 Å
- transition temperature increases with longer tail lengths and greater saturation (typically between 10 – 40° C)

eg. longer tails and more saturation favor ordered state

Cholesterol decreases transition temperature by inhibiting formation of the gel like state





Disordered or fluid (left) and Ordered (right) states of a bilayer

Bilayers and Temperature

The composition of bilayers changes as a function of temperature of growth

- **increasing fraction <u>longer</u> tailed and <u>saturated</u> lipids at higher temperature**

eg. 22% of lipid is saturated at 10 ºC (4/22 or 18% is 14:0)
56% of lipid is saturated at 40 ºC (8/56 or 14% is 14:0)

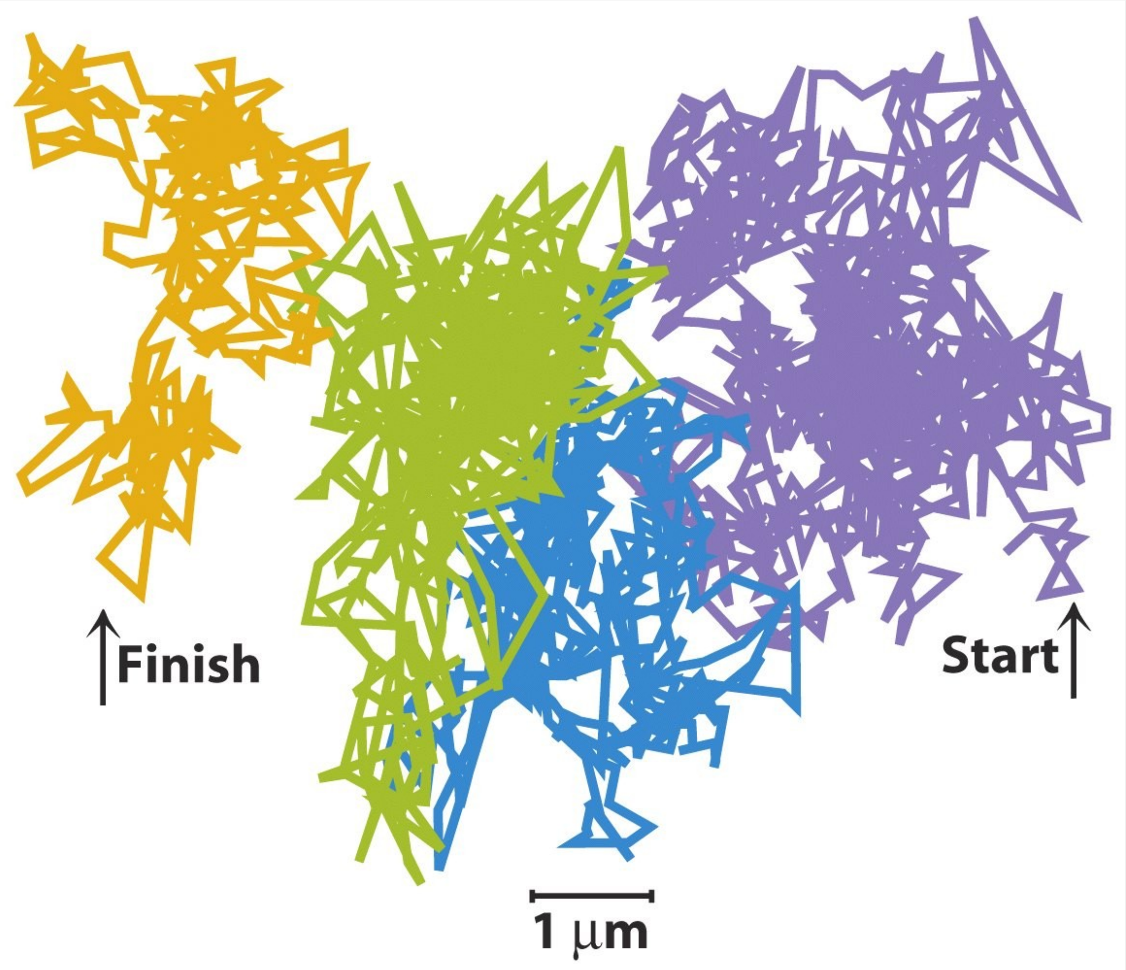
E. coli culture temperature

	Percentage of total fatty acids*			
	10 °C	*20 °C*	*30 °C*	*40 °C*
Myristic acid (14:0)	4	4	4	8
Palmitic acid (16:0)	18	25	29	48
Palmitoleic acid (16:1)	26	24	23	9
Oleic acid (18:1)	38	34	30	12
Hydroxymyristic acid	13	10	10	8
Ratio of unsaturated to saturated†	2.9	2.0	1.6	0.38

Explain this Result

The movement of a single labeled lipid on the cell surface

- recorded on video over 56 ms (fluorescent microscopy)
- starts in the purple area then moves through the blue, green and final the orange areas.

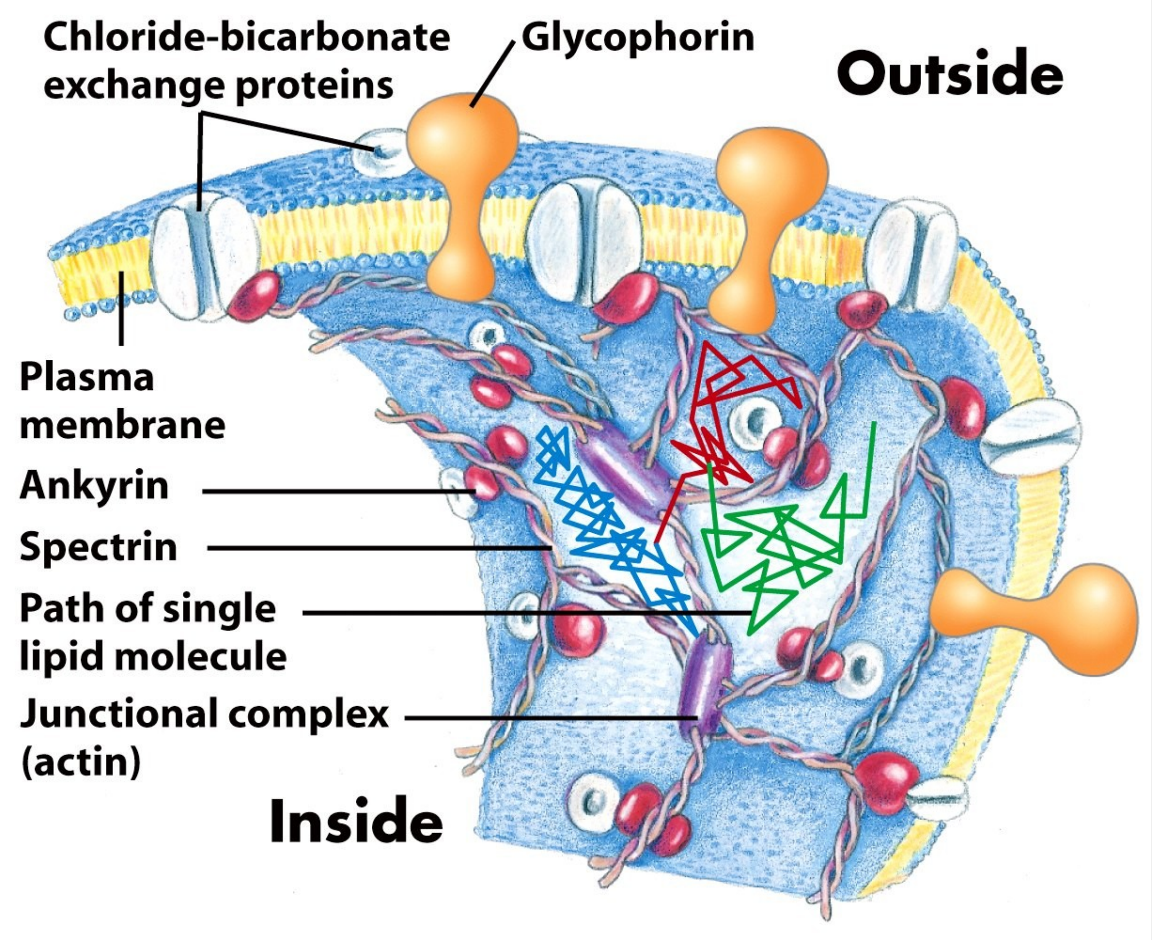


What's going on?

Membranes contain Proteins

The movement is restricted by membrane proteins

- Biological membranes contain significant quantities of protein
- Typical membranes have a protein:lipid ratio around 1:1



Membrane Composition (*eg.*)

Biological membranes contain a lot of proteins

Protein:Liped ratio varies between cell types

TABLE 12-4 Compositions of Some Biological Membranes

Membrane	Protein (%)	Lipid (%)	Carbohydrate (%)	Protein to Lipid Ratio
Plasma membranes:				
Mouse liver cells	46	54	2–4	0.85
Human erythrocyte	49	43	8	1.1
Amoeba	52	42	4	1.3
Rat liver nuclear membrane	59	35	2.0	1.6
Mitochondrial outer membrane	52	48	(2–4)[a]	1.1
Mitochondrial inner membrane	76	24	(1–2)[a]	3.2
Myelin	18	79	3	0.23
Gram-positive bacteria	75	25	(10)[a]	3.0
Halobacterium purple membrane	75	25		3.0

[a]Deduced from the analyses.

Membrane Proteins

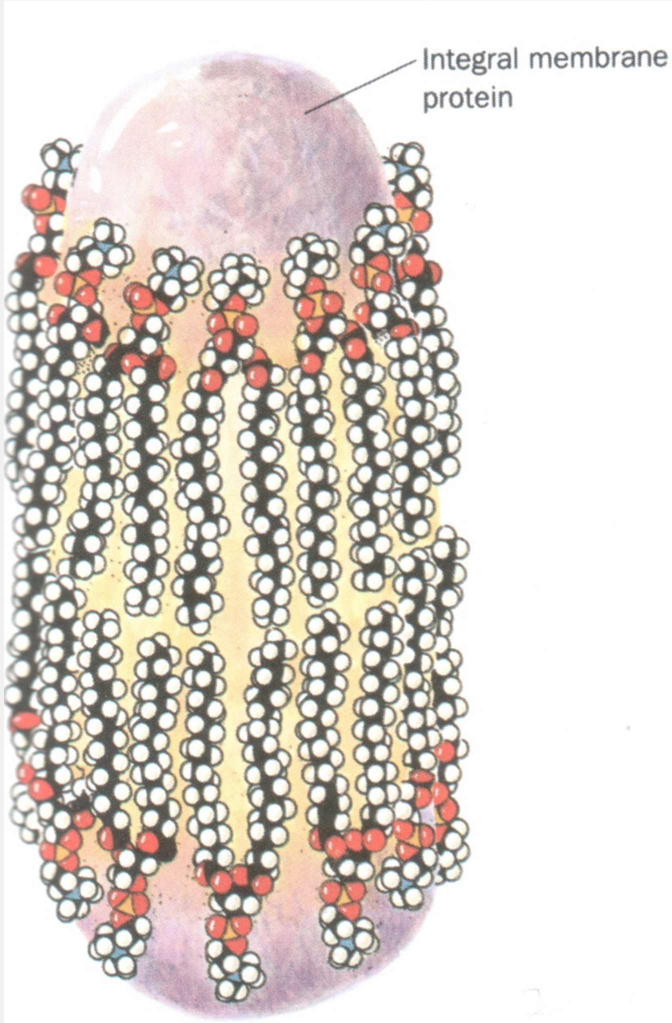
Two general classes of membrane proteins

(1) Integral or intrinsic membrane protein are tightly bound by hydrophobic forces

- must disrupt membrane (*ie.* detergents) to separate proteins

(2) Peripheral or extrinsic membrane proteins are anchored or associate with membranes

- can be separated by mild treatments that leave membranes intact

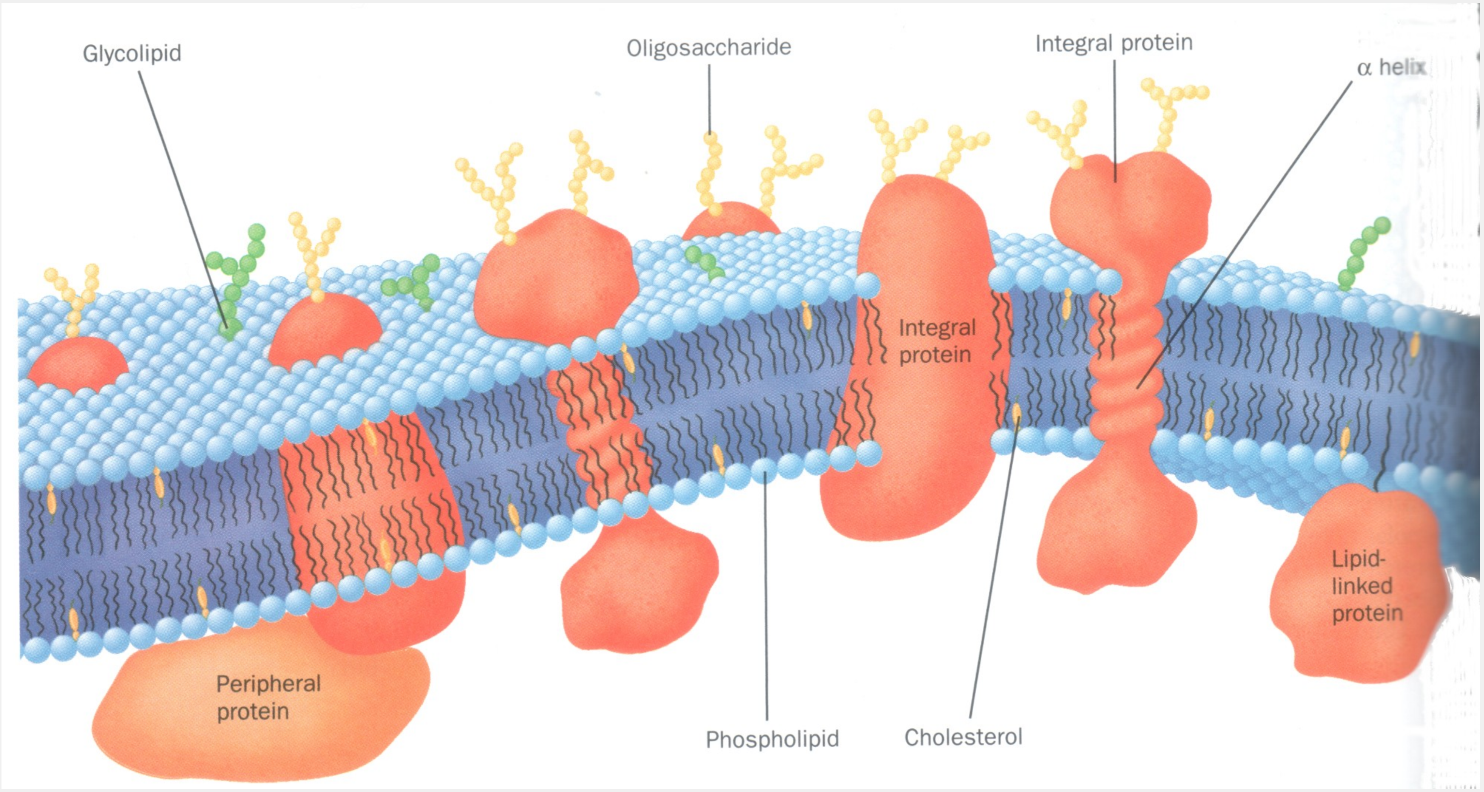


Membrane Proteins (more)

Integral membrane proteins are asymmetrically oriented

- **surface labeling identifies two distinct types of integral proteins**

  (1) transmembrane proteins that span the membrane and are exposed on both sides of the membrane



Membrane Proteins (cont.)

(2) **embedded** proteins that are only exposed on a specific side of the membrane

- anchored to membrane by polypeptide segment OR lipid modification

Lipid modification that anchor embedded proteins:

(1) isoprenoid groups

(2) fatty acyl groups

(3) glycoinositol phospholipids